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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,812	09/07/2001	Lan-Qing Huang	L0461.70115US00	3475

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
03/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/856,812	HUANG ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02/19/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,9-11,42-49 and 52-55* is/are pending in the application.

4a) Of the above claim(s) *10 and 51* is/are withdrawn from consideration.

5)☒ Claim(s) *4,5,9,42 and 43* is/are allowed.

6)☒ Claim(s) *1,2,11,44-49 and 52-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The finality of the previous Office action has been withdrawn, and the prosecution of this application is reopened to include new reasons for rejection raised upon further consideration.

Claims 1-2, 4-5, 9, 11, 42-49, 52-55 are examined in the instant application.

Withdrawn Rejection

The 112, first paragraph, enablement rejection of claims 4-5, 9, 42-43 has been withdrawn, in view of the submitted references by Huang et al, 1999, and Valmori et al, 2001, and the response arguments.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 11, 44-49, 52-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

The response submits the references by Huang et al, 1999, and Valmori et al, 2001. The response asserts that Valmori et al teach that CD8+ T cells directed against the peptide MAGE-10, amino acids 254-262, are detectable in a large proportion of HLA-A2+ melanoma patients, thus indicating that MAGE-10 protein is expressed in cancer.

The response has been considered but is not found to be persuasive for the following reasons:

Claims 1-2, 11, 44-49, 52-55 encompass sequences having unknown amino acids attached to the peptide consisting of 8-10 amino acids of SEQ ID NO:1, which sequences are capable of binding to MHC and elicit T cells response.

One cannot predict that the claimed sequences could bind to MHC and elicit T cells response, due to **the unpredictable effect** on MHC binding, and CTL recognition or activation **of unkown flanking sequences**, which effect could also depend and/or vary with the **size** of the amino acid sequence added to the CTL epitope. Bergmann et al, 1994 (J Virol, 68(8): 5306-5310) teach that CTL recognition of a 9 amino acid CTL epitope of the nucleocapsid protein (JN), even having immediate flanking sequences composed of its native sequence, varies, and depends on the size and/or composition of the flanking sequences (abstract , figures 1-2 on page 5307). For example, the longest sequence vtan 38 is most recognized as compared to the smaller sequences vtan 7, or vtan 2 (figures 1-2 on page 5307). Eisenlohr et al, 1992 (J Exp Med, 175: 481-487) teach that flanking sequences influence the presentation of a CTL peptide. Eisenlohr et al teach that addition of just two C-terminal native amino acids or ten native amino acids at the N- and C-termini all abolishes the CTL recognition (abstract, p. 484). Eisenlohr et al teach that any one or a combination of the following could be involved in the negative effects of flanking sequences: 1) Sequestration of the peptides on peptide binding proteins in the cytosol or exocytic compartment, 2) Inability of peptide intermediates to be transported from the cytosol to the exocytic compartment, 3) Inability of peptide intermediates to associate with accessory molecules that might function to deliver peptides to Class I molecule in the exocytic

compartment, or 4) Inability of cellular proteases to generate antigenic peptide from the protein or longer peptide (p. 485, first column, last paragraph). Shastri et al, 1995 (J Immunol, 155: 4339-4346) teach that presentation of CTL peptide is profoundly influenced by specific added C-terminal flanking residues. Shastri et al teach that of the five amino acids C, I, L, M, V that can serve as C-terminal anchors, three amino acids C, I, L are actually inhibitory to CTL recognition (p. 4343, first column). Shastri et al further teach that the extra amino acid could result in either an intervening bulge, or the flanking residue projecting out, and the accessibility to the carboxypeptidases could be affected, resulting in the low yield to processed antigenic CTL peptide (p. 4345, second paragraph). Guo et al, 1992 (Nature, 360: 364-366) teach that different length peptides bind to a HLA molecule similarly at their ends but bulge out in the middle. Thus in view of the teaching in the specification and in the art, one cannot predict that addition of unknown amino acids to the claimed 8-10 amino acids of SEQ ID NO:1 would not result in loosing CTL recognition, or binding affinity to MHC molecule due to the intervening bulging effect at the middle of the molecule, or the flanking residue(s) projecting out, and/or the loss of the accessibility to the carboxypeptidases.

MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In

constrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the claimed invention, it would have been undue experimentation for one of skill in the art to practice the claimed invention commensurate in scope of the claims.

Conclusion

Claims 4-5, 9, 42-43 seem to be free of prior art and are allowable.

Claims 1-2, 11, 44-49, 52-55 are rejected for reasons set forth above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
March 18, 2008

. /Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643